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Targeted Epigenetic Editing Using Optogenetic Tools

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ABSTRACT

Epigenetics markers, such as DNA methylation and histone post-translational modifications, are modifications to the structure of DNA that impact gene expression without altering the genetic code. Among them, DNA methylation plays a critical role in various biological processes including the differentiation of stem cells, regulation of gene expression, and adaptation to environmental signals. The ability to modify DNA methylation at particular genes in various cell types is thus desirable for engineering specific cell phenotypes. Although technologies exist that can alter DNA methylation at target genes, these techniques lack spatial and temporal resolution and are not able to selectively edit individual cells within a cell population, which poses issues when trying to create new disease models and understand cell development. In this work, we incorporate spatiotemporal control to epigenetic editing tools via the use of optogenetic proteins CIB1 and CRY2. CIB1 and CRY2 form a multimer when exposed to blue light of wavelength 390-480 nm. To create a targeted DNA methylation editing system, CIB1 was fused to dCas9, which guides the editing tool to the site of interest, while CRY2 was fused to DNMT3a, a DNA methyltransferase. Upon exposure to blue light, CRY2 is recruited to CIB1, bringing DNMT3a close to the targeted gene and adding DNA methylation at specific locations. This optically controlled system holds potential as it can be readily adapted to modify different genes and different epigenetic markers with spatiotemporal precision.
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KEYWORDS

Epigenetics, DNA methylation, CRISPR, Optogenetics